Metal Complexes of Biologically Important Ligands, CLXXI [1]. Incorporation of the *cis*-Dichloroplatinum Group into Amides of 3,4-Diarylpyrrole-2,5-dicarboxylic Acids

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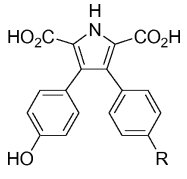
Dedicated to Professor Ingo-Peter Lorenz on the occasion of his 65th birthday

3,4-Bisarylpyrrole-2,5-dicarboxylic acids were coupled with *rac*-N^1,N^2-di-Boc-1,2,4-triaminobutane to give the corresponding diamides, which were deprotected and converted into the bis(*cis*-dichloroplatinum) complexes by treatment with K_2PtCl_4.

Key words: Pyrrole-2,5-dicarboxylic Acids, 1,2,4-Triaminobutane, Bis(ethylenediamine), *cis*-Dichloroplatinum Complexes

Introduction

3,4-Diarylpyrrole-2,5-dicarboxylic acids are suitable starting materials for the biomimetic synthesis of several types of marine pyrrole alkaloids, *e. g.* lamellarins [2], polycitrins [3], polycitones [4], and storniamides [5]. Several of these compounds exhibit interesting anticancer activities [6], and even the simple pyrrole dicarboxylic acids **1** and **2**, isolated from a marine *Halomonas* bacterium, show remarkable antitumor-promoting properties [7]. It seemed therefore attractive to us to use pyrroledicarboxylic acids as templates for ethylenediamine ligands, which could be easily transformed into the corresponding di(platinum) complexes.



1, R = H
2, R = OH

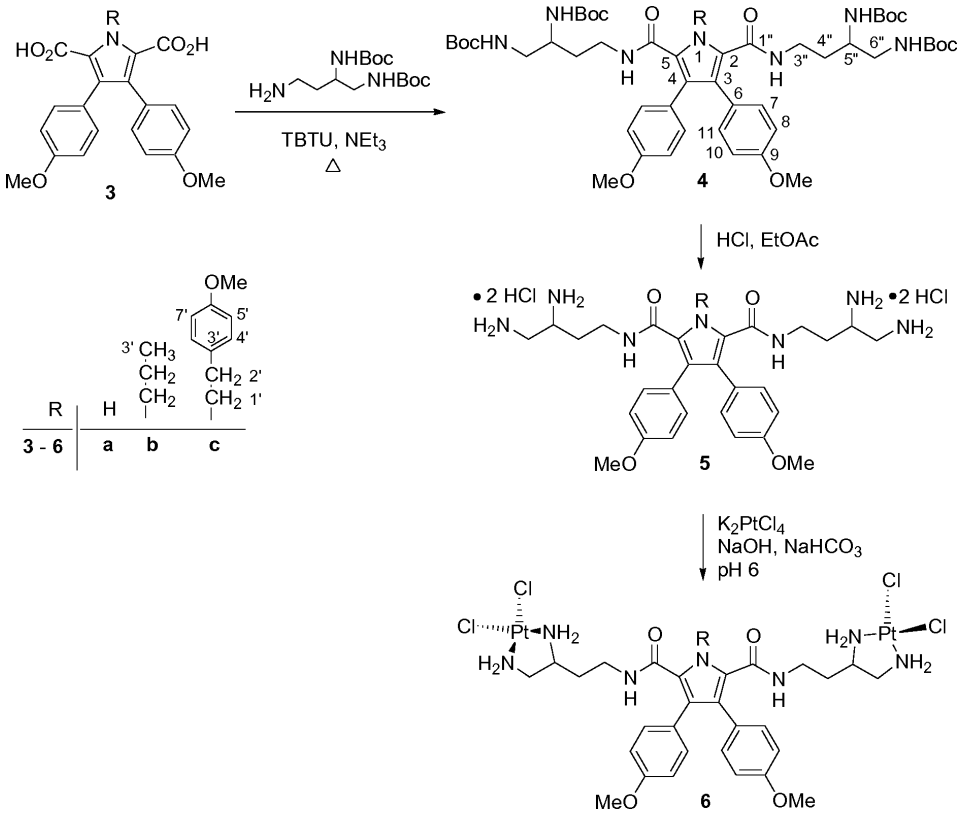
At present di- and multinuclear platinum complexes find much interest as a novel class of anticancer agents [8], which may circumvent cisplatinum resistance and which have been studied particularly well by Farrell and coworkers [9]. Our group has contributed some examples of diplatinum complexes [10, 11]. Moreover it appears possible that the diarylpyrrole core could intercalate into DNA. This concept of attaching cytotoxic groups to DNA-affine compounds – a combination of two strategies for cancer therapy – has been followed by several authors [12].

Results and Discussion

The 3,4-bis-(4-methoxyphenyl)pyrrole-2,5-dicarboxylic acids **3a** – **c** were synthesized by converting 3-(4-methoxyphenyl)pyruvic acid with *n*-BuLi into its dianion, followed by oxidative dimerization with iodine and condensation of the 1,4-diketone intermediate with ammonia, *n*-propylamine or 2-(4-methoxyphenyl)ethylamine, respectively [2, 3, 13] (Scheme 1).

Following a strategy introduced by Altman in our group for the synthesis of various alkane-α,ω-dicarboxylic acid amides with terminal ethylenediamine groups [10, 11a], the pyrroledicarboxylic acids **3a** – **c** were coupled with *rac*-1,2-Boc protected 1,2,4-triaminobutane [10a, 11a], to yield the diamides **4a** – **c** as 1 : 1-mixtures of diastereomers due to the chiral centers at position 5″ in the amide side chains. After acidolysis of the protecting groups, the resulting hydrochlorides **5a** – **c** were dissolved in water and treated at pH $\sim$ 6 under potentiometer control with K_2PtCl_4 to yield the bis(platinum) complexes **6a** – **c**.

We tried to improve the very low solubility of complex **6a** in water by converting it into the bis[dihydr-



Scheme 1.

oxydichloroplatinum (IV)] complex with H_2O_2 [14] which was, however, again almost insoluble in water. This prevented the evaluation of these compounds in biological tests.

In the IR spectra of **6a**–**c** characteristic absorptions are found at ν = 320 (PtCl), 3200 (NH), 1530 (NH), and 1650 cm^{-1} (CONH). The NMR spectra of these compounds correspond to those of their triaminobutane [10] and pyrroledicarboxylic acid units [2, 3]. In the ESI mass spectrum of **6b**, the molecular peak and a fragment resulting from cleavage of $Cl_2Pt(en)$ were detected.

Experimental Section

Melting points (uncorrected): Mel. Temp. (Laboratory Devices, Cambridge). IR spectra: Nicolet 520 FT-IR-spectrometer. Abbreviations: s, strong; m, medium; w, weak; br, broad. Mass spectra (EI 70 eV): Finnigan MAT 90 and Finnigan MAT 95Q. NMR spectra: Joel EX 400. The spectra were recorded in $CDCl_3$, [D_6]DMSO or [D_6]acetone using the residual solvent peak as an internal standard ($CDCl_3$, δ_H = 7.26 and δ_C = 77.10; [D_6]DMSO, δ_H = 2.49 and δ_C = 39.50; [D_6]acetone, δ_H = 2.04 and δ_C = 29.80). Elemental analyses were carried out by the Microanalytical Laboratory of our Department (Heraeus VT). Column chromatography: Merck Kieselgel 60 (0.063−0.200 mm). TLC: silica gel 60 F_{254} (Merck).

The pyrroledicarboxylic acids **3a** and **3c** were obtained as described in refs. [3a] resp. [3b]. *rac*-N^1,N^2-Dibenzyloxycarbonyl-1,2,4-triaminobutane was synthesized from *N*-trifluoroacetylhistidine [10a, 11a]. Recently, methods for the synthesis of this selectively protected butanetriamine in optically pure form were reported [10, 15]. *O*-(Benzotriazol-1-yl)-*N,N,N′,N′*-tetramethyluronium tetrafluoroborate (TBTU) was purchased from Bachem.

*3,4-Bis[(4-methoxyphenyl)-1-(2-n-propyl)]pyrrole-2,5-dicarboxylic acid (**3b**)*

A solution of 3-(4-methoxyphenyl)pyruvic acid (1 g, 5.2 mmol) [16] in dry THF (50 mL) was cooled to −78 °C, and *n*-BuLi (4.15 mL of a 2.5 M solution in hexane, 10.3 mmol) was added. After stirring for 20 min, a solution of iodine (0.65 g, 2.6 mmol) in dry THF (8 mL) was added dropwise. The mixture was allowed to warm up to 20 °C and, after the addition of *n*-propyl amine (1.54 g, 2.14 mL, 26 mmol), stirred with molecular sieves (4 Å) for 12 h. The reaction

was quenched with 2 N NaOH, and the resulting mixture washed with EtOAc (3×). After adjusting the pH to 4 with conc. HCl, the aqueous phase was extracted with EtOAc (3×). The combined organic phases were dried ($MgSO_4$) and concentrated under reduced pressure. Recrystallization from MeOH furnished **3b** (862 mg, 81 %) as colorless crystals. M. p. 268 – 270 °C. – IR (KBr): ν = 3700 (sh), 2980 (s), 2540 (m), 2040 (w), 1890 (w), 1720 (s), 1670 (s), 1620 (s), 1545 (s), 1430 (s), 1360 (m), 1300 (s), 1250 (s), 1120 (w), 1040 (s), 910 (w), 855 (s), 790 (s), 750 (w), 690 (w) cm^{-1}. – ^1H NMR ([D_6]DMSO, 400 MHz): δ = 0.84 (t, J = 14.8 Hz, 3H, 3′-H), 1.73 (sext, J = 14.8 Hz, 2H, 2′-H), 3.67 (s, 6H, 2 OCH_3), 4.59 (t, J = 14.8 Hz, 3H, 1′-H), 6.71 (d, J = 8.8 Hz, 4H, 8/10-H), 6.91 (d, J = 8.8 Hz, 7,11-H), 12.60 (br s, 2H, CO_2H). – ^{13}C NMR [(D_6]DMSO, 101 MHz): δ = 162.7 (CO_2H), 157.6 (C-9), 131.4 (CH-7/11), 128.9 (C-6), 126.8 (C-3/4), 124.4 (C-2/5), 112.6 (CH-8/10), 54.8 (OCH_3), 47.5 (CH_2-1′), 24.9 (CH_2-2′), 11.0 (CH_3-3′). – EIMS (230 °C): *m/z* (%) = 410 (24) $[M + H]^+$, 409 (100) $[M]^+$, 366 (15) $[M-C_3H_7]^+$, 365 (61) $[M-CO_2]^+$, 332 (12), 321 (42). – HREIMS: *m/z* = 409.1522 (calcd. 409.1518 for $C_{23}H_{23}NO_6$, $[M]^+$).

General method for the synthesis of ***4a – c***

To a solution of the pyrroledicarboxylic acids **3a – c** (1 equiv.) in acetonitrile (5 mL) maintained at 0 °C, *rac*-4-amino-1,2-di(*tert*-butoxycarbonylamino)butane (2 equiv.), NEt_3 (4 equiv.) and TBTU (2 equiv.) were added. After 2 h, the mixture was warmed to r. t. and stirred for 12 h (DC control: SiO_2, $CHCl_3$/MeOH, 10 : 1 v/v, blue fluorescence). The resulting mixture was heated under reflux for 1 h, stirred for 30 min and concentrated *in vacuo*. The residue was dissolved in EtOAc and the solution shaken with 1.1 M aqueous $KHSO_4$ (3×), saturated aqueous $NaHCO_3$ (3×) and saturated aqueous NaCl (1×). The organic phase was dried ($MgSO_4$) and concentrated *in vacuo*. The brown crude products were purified by chromatography (SiO_2, $CHCl_3$/MeOH, 10 : 1 v/v) and recrystallized from EtOAc/*n*-hexane to yield compounds **4a – c** as colorless products.

4a: From **3a** (750 mg, 2.0 mmol), *rac*-1,2-di(*tert*-butoxycarbonylamino)-4-aminobutane (1.23 g, 4.1 mmol), NEt_3 (1.23 mL, 8.12 mmol), and TBTU (1.3 g, 4.1 mmol). – Yield 1.55 g (81 %). – M. p. > 60 °C (dec.). – IR (KBr): ν = 3414 (s, br, NH), 2975 (s), 2938 (s), 2842 (m, OCH_3), 1706 (s, CO), 1652 (s), 1613 (m), 1574 (w), 1550 (s, δ NH), 1531 (s, br), 1445 (m), 1443 (sh), 1393 (s), 1367 (s), 1340 (w), 1289 (s), 1250 (s), 1175 (s), 1108 (m), 1065 (m), 1033 (m), 903 (w), 867 (w), 836 (m, ρ NH), 780 (m), 781 (m), 638 (m), 544 (m), 477 (w), 464 (w), 406 (w), 388 (w), 331 (w) cm^{-1}. – ^1H NMR (400 MHz, [D_6]acetone): δ = 8.01 (“s”, 2H, 2″-NH), 7.13 (d, ^3J = 8.7 Hz, 4H, 7/11-H), 6.87 (d, ^3J = 8.7 Hz, 4H, 8/10-H), 6.30 (m, 2H, 5″-NH), 6.04 (m, 1H, 6″-NH)*, 5.82 (m, 1H, 6″-NH)*, 3.76 (s, 6H, OCH_3), 3.48 (m, 4H, 3″-H), 3.09 (br m, 2H, 5″-H), 2.91 (m, 4H, 6″-H), 1.59 (br m, 4H, 4″-H), 1.40 (s, 18H, CH_3), 1.36 (s, 18H, CH_3) (*diastereomers). – ^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.8, 159.0, 156.9, 156.3, 132.0 (CH), 125.9, 125.4, 114.2 (CH), 79.5, 79.2, 55.1 (CH_3), 49.5 (CH-5″), 44.4 (CH_2-6″), 36.0 (CH_2-3″), 32.9 (CH_2-4″), 28.4 (CH_3), 28.3 (CH_3) (one signal obscured or overlapping). – $C_{48}H_{71}N_7O_{12}$ (938.09): calcd. C 61.46, H 7.63, N 10.45; found C 60.91, H 7.64, N 10.05.

4b: From **3b** (762 mg, 1.86 mmol), *rac*-1,2-di(*tert*-butoxycarbonylamino)-4-aminobutane (1.19 g, 3.92 mol), NEt_3 (1.04 mL, 7.45 mmol), and TBTU (1.20 g, 3.72 mmol). – Yield 1.39 g (76 %). – M. p. > 60 °C (dec.). – IR (KBr): ν = 3404 (br, ν NH), 3001 (sh), 2975 (m), 2934 (m), 2876 (w), 2841 (w), 1702 (s, COO), 1649 (m, CON), 1615 (sh), 1574 (sh), 1530 (s, δ NH), 1456 (m), 1443 (sh), 1405 (sh), 1392 (m), 1367 (s), 1303 (sh), 1287 (m), 1273 (w), 1247 (s), 1175 (s), 1109 (w), 1067 (w), 1035 (m), 1000 (w), 901 (w), 868 (w), 836 (m, ρ NH), 792 (m), 783 (m), 748 (w), 596 (w), 537 (w), 464 (w), 329 (sh) cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ = 6.99 (d, ^3J = 6.0 Hz, 4H, 7/11-H), 6.70 (d, ^3J = 8.4 Hz, 4H, 8/10-H), 6.45−6.37 (m, 2H, NH), 5.02 (m, 2H, NH), 4.86 (d, ^3J = 7.1 Hz, 1H, NH), 4.45−4.21 (m, 3H, NH, 1′-H), 3.72 (s, 6H, OCH_3), 3.69−3.63 (m, 4H, 3″-H), 3.05 (m, 2H, 5″-H), 2.73−2.55 (m, 4H, 6″-H), 1.81−1.75 (m, 4H, 4″-H), 1.55 (m, 2H, 2′-H), 1.38 (s, 18H, CH_3), 1.29 (s, 18H, CH_3), 0.89 (t, ^3J = 7.2 Hz, H, 3′-H). – ^{13}C NMR (101 MHz, $CDCl_3$): δ = 162.3, 158.0, 156.7, 132.0 (CH), 127.1, 126.7, 124.2, 123.9, 113.6 (CH), 79.5, 79.1, 55.2 (OCH_3), 49.6 (CH_2), 47.8 (CH), 44.3 (CH_2), 35.4 (CH_2), 33.3 (CH_2), 28.4 (CH_3), 28.3 (CH_3), 25.5 (CH_2), 11.4 (CH_3). – $C_{51}H_{77}N_7O_{12}$ (980.21): calcd. C 62.49, H 7.92, N 10.00; found C 62.60, H 8.17, N 9.46.

4c: From **3c** (1.02 g, 2.17 mmol), *rac*-1,2-di(*tert*-butoxycarbonylamino)-4-amino-butane (1.32 g, 4.35 mmol), NEt_3 (1.28 mL, 8.71 mmol), and TBTU (1.4 g, 4.36 mmol). – Yield 305 mg (62 %). – M. p. > 60 °C (dec.). – IR (KBr): ν = 3414 (m), 3243 (s, br, NH), 2975 (s), 2938 (s), 2838 (m, OCH_3), 1705 (s, CO), 1653 (s), 1612 (m), 1575 (w), 1551 (s, δ NH), 1530 (s, br), 1445 (m), 1442 (sh), 1392 (s), 1367 (s), 1341 (w), 1290 (s), 1250 (s), 1174 (s), 1109 (m), 1065 (m), 1033 (m), 902 (w), 868 (w), 835 (m, ρ NH), 781 (m), 639 (m), 542 (m), 477 (w), 465 (w), 411 (w), 406 (w), 393 (w), 383 (w), 331 (w) cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ = 7.17 (d, ^3J = 8.6 Hz, 2H, 4′/8′-H), 7.04 (d, ^3J = 8.5 Hz, 4H, 7/11-H), 7.03 (d, ^3J = 8.6 Hz, 2H, 5′/7′-H), 6.81 (d, ^3J = 8.5 Hz, 4H, 8/10-H), 6.38 (br s, NH), 6.18 (br s, NH), 4.99 (br d, NH), 4.84 (br d, NH), 4.69 (t, 2H, 1′-H), 3.77 (s, 9H, OCH_3), 3.64 (m, 4H, 3″-H), 3.11 (m, 5″-H), 2.77 (m, 4H, 6″-H), 2.61 (m, 2H, 2′-H), 1.83−1.74 (m, 4H, 4″-H), 1.50 (s, 18H, CH_3), 1.34 (s, 18H, CH_3). – ^{13}C NMR (101 MHz, $CDCl_3$): δ = 162.5, 158.5, 157.2,

157.0, 132.3 (4C, CH-7/11), 131.6, 130.7 (2C, CH-4′/8′), 127.3, 127.2, 124.17, 124.16, 114.1 (4C, CH-8/10), 114.0 (2C, CH-5′/7′), 79.9, 79.4, 55.64 (OCH_3), 55.56 (OCH_3), 50.0 (CH_2-1′), 48.5 (CH-5″), 44.6 (CH_2-6″), 38.1 (CH_2-2′), 35.8 (CH_2-3″), 33.7 (CH_2-4″), 28.8 (CH_3), 28.6 (CH_3). – EIMS: *m/z* (%) = 1072(0.5) $[M]^+$, 743 (13), 440 (12), 135 (9). – FABMS: *m/z* (%) = 1072 (11) $[MH]^+$, 185 (70), 135 (31), 93 (100). – FAB MS: *m/z* (%) = 1071 (21) $[M]^+$, 786 (18), 183 (100), 91(49). – ESIMS: *m/z* (%) = 1110 (12) $[M + Kr]^+$, 1096 (39), 1095 (66), 1094 (100) $[M + Na]^+$, 974 (15), 973 (31), 972 (61), 962 (10). – HRESIMS calcd. for $[M + Na]^+$: 1094.5790, found: 1094.5793. – $C_{57}H_{81}N_7O_{13}$ (1072.28): calcd. C 63.84, H 7.61, N 9.14; found C 63.74, H 7.52, N 9.11.

General method for the synthesis of the hydrochlorides ***5a – c***

To a solution of **4a – c** in EtOAc (3 mL), EtOAc saturated with HCl (10 mL), was added. Gas evolution occurred, and after 2 h a colorless precipitate was formed, which was washed with EtOAc (3×) and dry Et_2O (1×) and dried *in vacuo*.

5a: From **4a** (300 mg, 0.323 mmol). – Yield 210 mg (95 %). – IR (KBr): ν = 3399 (s, br, ν NH), 3011 (s), 2960 (s), 2835 (s, OCH_3), 2044 (w), 1971 (w), 1905 (w), 1629 (s, br, CO), 1610 (s, CO), 1575 (s, δ NH), 1555 (s), 1530 (s), 1506 (s), 1465 (s), 1444 (m), 1409 (w), 1374 (w), 1304 (s), 1290 (s), 1249 (s), 1178 (s), 1111 (w), 1032 (m), 994 (w), 957 (w), 836 (m, ρ NH), 800 (w), 793 (w), 779 (w), 543 (m), 476 (w) cm^{-1}. – ^1H NMR (400 MHz, D_2O): δ = 6.97 (d, ^3J = 8.2 Hz, 4H, 7/11-H), 6.69 (d, ^3J = 8.2 Hz, 4H, 8/10-H), 3.59 (s, 6H, OCH_3), 3.41 – 3.15 (m, 10H, 3″-H, 5″-H, 6″-H), 1.93 (m, 2H, 4″-H). – ^{13}C NMR (101 MHz, D_2O): δ = 163.4 (C-1″), 158.6, 132.1 (CH), 127.5, 125.2, 124.0, 114.2 (CH), 55.4 (OCH_3), 47.5 (CH), 41.1 (CH_2), 35.3 (CH_2), 30.5 (CH_2). – $C_{28}H_{43}Cl_4N_7O_4{\cdot}2H_2O$ (719.50): calcd. C 46.74, H 6.58, N 13.63; found C 46.61, H 6.70, N 13.20.

5b: From **4b** (300 mg, 0.310 mmol). – Yield 182 mg (81 %). – IR (KBr): ν = 3407 (s, ν NH), 3033 (br), 2835 (br), 2660 (sh), 2579 (sh), 2037 (m), 1986 (w), 1891 (w), 1633 (s, CON), 1613 (s), 1576 (s), 1530 (s, δ NH), 1499 (s), 1464 (s), 1410 (m), 1356 (m), 1306 (m), 1289 (s), 1249 (s), 1179 (s), 1161 (sh), 1110 (m), 1031 (s), 960 (w), 904 (w), 838 (s, ρ NH), 792 (m), 741 (w), 594 (w), 540 (m), 477 (w) cm^{-1}. – ^1H NMR (400 MHz, D_2O): δ = 7.08 (d, ^3J = 7 Hz, 4H, 7/11-H), 6.85 (d, ^3J = 7 Hz, 4H, 8/10-H), 4.22 (t, ^3J = 6.8 Hz, 2H, 1′-H), 3.74 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 3.44 (quint, ^3J = 5.8 Hz, 2H, 5″-H), 3.33 – 3.28 (m, 4H, 3″-H), 3.27 – 3.23 (m, 4H, 6″-H), 1.75 (q, ^3J = 7.3 Hz, 4H, 4″-H), 1.67 (m, ^3J = 7.2 Hz, 2H, 2′-H), 0.77 (t, ^3J = 7.2 Hz, 3H, 3′-H). – ^{13}C NMR (101 MHz, D_2O): δ = 165.2 (C-1″), 158.1, 131.9, 131.7, 127.2 (4C, CH-7/11), 126.0 (2C), 125.6 (4C), 113.56 (2C, CH-8/10), 113.50 (2C, CH-8/10)*, 55.7 (OCH_3), 55.1 (OCH_3)*, 47.72 (C-5″), 47.68 (C-5″)*, 47.1 (CH_2-1′), 40.8 (CH_2-6″), 35.4 (CH_2-3″), 29.7 (CH_2-4″), 24.7 (CH_2-2′), 10.6 (CH_3-3′) (*diastereomers). – $C_{31}H_{49}Cl_4N_7O_4{\cdot}2H_2O$ (761.55): calcd. C 48.89, H 7.01, N 12.87; found C 48.74, H 7.04, N 12.38.

5c: From **4c** (203 mg, 0.189 mmol). – Yield 145 mg (94 %). – IR (KBr): ν = 3359 (s, br, ν NH), 301 (s), 2961 (s), 2836 (s, OCH_3), 1618 (s, CO), 1565 (s, δ NH), 1552 (s), 1531 (s), 1507 (s), 1460 (s), 1442 (m), 1405 (w), 1375 (w), 1303 (s), 1290 (s), 1249 (s), 1179 (s), 1110 (w), 1033 (m), 995 (w), 961 (w), 834 (m, ρ NH), 801 (w), 790 (w), 779 (w), 542 (m), 476(w) cm^{-1}. – ^1H NMR (D_2O): δ = 6.93 (d, ^3J = 8.3 Hz, 4H, 7/11-H), 6.77 – 6.66 (m, 4H, 8/10-H), 3.62 (s, 2H, 1′-H), 3.54 (s, 9 H, OCH_3), 3.26 (m, 4H, 3″-H), 3.13 (m, 2H, 5″-H), 3.01 (m, 4H, 6″-H), 2.72 (m, 2H, 2′-H), 1.52 (m, 4H, 4″-H). – ^{13}C NMR (D_2O): δ = 164.9 (C-1″), 158.9, 158.4, 132.4, 131.5, 131.0, 128.0, 126.9, 126.3, 114.6, 114.4, 56.0 (OCH_3), 55.8 (OCH_3), 48.1 (CH_2-1′), 47.8 (CH-5″), 41.4 (CH_2-6″), 37.2 (CH_2-2′), 35.8 (CH_2, C-3″), 30.1 (CH_2, C-4″). – $C_{37}H_{53}Cl_4N_7O_5{\cdot}H_2O$ (835.64): calcd. C 54.35, H 9.92, N 11.99; found C 54.23, H 10.15, N 11.89.

General method for the synthesis of platinum complexes ***6a – c***

To a solution of **5a – c** in water (2 mL), the stoichiometric amount of K_2PtCl_4 (dissolved in a very small amount of water) was added, and the solution was heated to 65 °C. After cooling, about 90 % of the hydrochloride was neutralized with 1 M NaOH and the resulting solution adjusted to pH = 5.5 with 1 M $NaHCO_3$ under potentiometer control. During the neutralization, the products were obtained as pale beige precipitates, which were centrifuged off, washed with ice cold water (3×) and cold EtOH (1×), and dried *in vacuo*.

6a: From **5a** (187 mg, 0.274 mmol), K_2PtCl_4 (227 mg, 0.548 mmol), 1 M NaOH (0.98 mL), and 1 M $NaHCO_3$ (0.12 mL). – Yield 215 mg (73 %). – M. p. > 200 °C (dec.). – IR (KBr): ν = 3399 cm^{-1} (s, br), 3370 (sh), 3216 (s, ν NH), 3121 (s), 2945 (s), 2842 (s, OCH_3), 2535 (w), 2037 (w), 1637 (s, CO), 1613 (s, CO), 1576 (s), 1554 (s, δ NH), 1530 (s), 1505 (s), 1462 (m), 1442 (m), 1408 (w), 1366 (w), 1303 (s), 1290 (sh), 1248 (s), 1179 (s), 1143 (w), 1108 (w), 1028 (m), 836 (m, ρ NH), 799 (w), 792 (w), 779 (w), 547 (m, Pt–N), 469 (w), 440 (w), 402 (w), 320 (m, Pt–Cl), 298 (sh, Pt–Cl). – ^1H NMR (400 MHz, [D_6]DMSO): δ = 11.82 (s, 2H, NH), 6.97 (d, ^3J = 7.5 Hz, 4H, 7/11-H), 6.81 (d, ^3J = 7.5 Hz, 4H, 8/10-H), 6.23 – 5.93 (m, 2H, NH), 5.43 (m, 1H, NH), 5.26 – 5.16 (m, 1H, NH), 3.73 (s, 6H, OCH_3), 3.18 (m, 4H, 3″-H), 2.61 (m, 2H, 5″-H), 2.35 (m, 2H, 6″-H), 2.13 (m, 2H, 6″-H), 1.62 (br m, 4H, 4″-H). – $C_{28}H_{39}Cl_4N_7O_4Pt_2{\cdot}H_2O$ (1087.59): calcd. C 30.92, H 3.79, N 9.01; found C 31.05, H 4.09, N 8.51.

6b: From **5b** (100 mg, 0.138 mmol), K_2PtCl_4 (114 mg, 0.276 mmol), 1 M NaOH (0.49 mL), and $NaHCO_3$ (0.05 mL). – Yield 121 mg (79 %). – IR (KBr): ν = 3464 (sh), 3409 (m), 3210 (s, ν NH), 3115 (m), 2961 (m), 1938 (m), 2875 (sh, br, OCH_3), 2839 (w), 1642 (s, CON), 1613 (sh), 1576 (m), 1530 (s, δ NH), 1499 (m), 1457 (m), 1443 (sh), 1410 (w), 1355 (w), 1305 (m), 1288 (m), 1247 (s), 1180 (m), 1156 (w), 1138 (w), 1108 (w), 1094 (sh), 1027 (m), 971 (w), 942 (w), 906 (w), 871 (w), 837 (m, ρ NH), 793 (m), 745 (w), 652 (w), 605 (w), 593 (w), 543 (m, Pt–N), 467 (w), 320 (m, Pt–Cl) cm^{-1}. – ^1H NMR (400 MHz, [D_6]DMSO): = 7.85 – 7.68 (m, 2H, NH), 6.91 (m, 4H, 7/11-H), 6.81 (m, 4H, 8/10-H), 5.39 (4H, NH), 5.18 – 5.11 (s, 4H, NH), 4.06 (m, 2H, 1′-H), 3.71 (s, 6H, OCH_3), 3.06 (m, 4H, 3″-H), 2.42 (m, 2H, 5″-H), 2.27 (m, 2H, 6″-H), 2.11 (m, 2H, 6″-H), 1.66 (m, 4H, 4″-H), 1.53 (m, 2H, 2′-H), 0.85 (m, 3H, 3′-H). – $C_{31}H_{44}Cl_4N_7O_4Pt_2 \cdot H_2O$ (1129.68): calcd. C 32.96, H 4.10, N 8.68; found C 32.92, H 4.37, N 8.56.

6c: From **5c** (154 mg, 0.187 mmol), K_2PtCl_4 (227 mg, 0.547 mmol), 1 M NaOH (0.67 mL), and 1 M $NaHCO_3$ (0.07 mL). – Yield 119 mg (53 %). – IR (KBr): ν = 3478 (s), 3409 (s, ν NH), 3206 (s, ν NH), 3116 (s), 3003 (sh), 2934 (s), 2838 (s, OCH_3), 2539 (w), 2374 (w), 2043 (w), 1899 (w), 1641 (s, CO), 1612 (s, CO), 1576 (s), 1530 (s, δ NH), 1513 (s), 1501 (s), 1456 (s), 1442 (s), 1410 (sh), 1368 (w), 1352 (m), 1302 (s), 1289 (s), 1246 (s), 1179 (s), 1155 (w), 1110 (m), 1028 (s), 940 (w), 915 (w), 875 (w), 838 (m, ρ NH), 815 (w), 793 (w), 779 (w), 750 (w), 702 (w), 634 (w), 609 (w), 595 (w), 539 (m, Pt–N), 473 (w), 391 (w), 321 (m, Pt–Cl) cm^{-1}. – ^1H NMR (400 MHz, [D_6]DMSO): δ = 11.85 (s, 2H, NH), 6.96 (d, ^3J = 7.1 Hz, 4H, 7/11-H), 6.81−6.66 (m, 8H, 8/10, 4′/8′, 5′/7′-H), 6.23−5.93 (m, 2H, NH), 5.43 (m, 1H, NH), 5.26 – 5.16 (m, 1H, NH), 4.57 (m, 2H, 1′-H), 3.73 (s, 9H, OCH_3), 3.18 (m, 4H, 3″-H), 3.10 (m, 2H, 5″-H), 2.61 (m, 2H, 2′-H), 2.35 (m, 2H, 6″-H), 2.23 (m, 2H, 6″-H), 1.62 (br m,, 4H, 4″-H). – ES-IMS (3 kV): *m/z* (%) = 1228 (9) $[MH_2 + Na]^+$, 1226 (11) $[M + Na]^+$, 903 (17) [M – $Pt(en)Cl_2$], 578 (10), 572 (65), 414 (33), 302 (100). – $C_{37}H_{49}Cl_4N_7O_5Pt_2 \cdot H_2O$ (1221.77): calcd. C 36.37, H 4.21, N 8.02; found C 36.68, H 4.48, N 8.01.

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